# o-NITROANISOLE CAS No. 91-23-6

First Listed in the Eighth Report on Carcinogens

$$O_2N$$
 $O$ 
 $CH_3$ 

# **CARCINOGENICITY**

o-Nitroanisole is reasonably anticipated to be a human carcinogen based on sufficient evidence of malignant tumor formation at multiple tissue sites in multiple species of experimental animals (NTP, 1993).

When administered in the diet to male and female rats, *o*-nitroanisole induced increased incidences of mononuclear cell leukemia and neoplasms of the urinary bladder, kidney, and large intestine. When administered in the diet to male and female mice, *o*-nitroanisole induced increased incidences of benign and malignant hepatocellular neoplasms in males and increased incidences of hepatocellular adenomas in females.

There are no adequate data available to evaluate the carcinogenicity of *o*-nitroanisole in humans.

# ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

o-Nitroanisole is genotoxic in a wide variety of assays in bacteria and mammalian cells and mutagenic and carcinogenic metabolites have been described (IARC V.65, 1996; NTP, 1993).

No data are available that would suggest that the mechanisms thought to account for tumor induction by o-nitroanisole in experimental animals would not also operate in humans.

# **PROPERTIES**

o-Nitroanisole is a colorless to slightly yellow liquid with a boiling point of 277°C and a melting point of 9.4°C. It is insoluble in water but is soluble in most organic solvents, including alcohol and ether. As a bulk chemical, o-nitroanisole is stable for two weeks at temperatures up to 60°C when stored protected from light. When heated to decomposition, o-nitroanisole emits toxic fumes of  $NO_x$ .

## **USE**

o-Nitroanisole is used primarily as a precursor to o-anisidine which is prepared by direct nitro-reduction. o-Anisidine is used extensively in the synthesis of azo dyes either directly after being converted to a diazonium salt or as a precursor for the preparation of dianisidine which is diazotized and coupled. Directly or indirectly, o-anisidine is used in the manufacture of over 100 azo dyes (NTP, 1993). o-Nitroanisole has also been used as an intermediate for pharmaceuticals (IARC V.65, 1996).

## **PRODUCTION**

o-Nitroanisole is produced by treating 2-chloronitrobenzene with sodium methoxide under heat and pressure. The product separates as an oil after dilution with water (IARC, 1996). Of the 5 U.S. plants reporting production or import use of o-nitroanisole in the 1977 TSCA Inventory, the 1 known manufacturer reported a production volume of 100,000 to 1,000,000 lb/year (TSCAPP, 1983 update), the 3 known importers did not report volume information, and 1 plant's role was unknown. In 1976 and 1978, imports of the compound through principal U.S. customs districts were reported to total 702,643 and 541,850 lb, respectively (HSDB, 1993). No current data on imports or exports of o-nitroanisole were available. Chem Sources (1996) identified 15 U.S. suppliers of o-nitroanisole.

#### **EXPOSURE**

The primary routes of potential human exposure to *o*-nitroanisole are dermal contact, ingestion, and inhalation. Human exposure might be associated with its widespread use in the manufacture of azo dyes (NTP, 1993). *o*-Nitroanisole was not included in the National Occupational Hazard Survey or the National Occupational Exposure Survey conducted by NIOSH (1990). *o*-Nitronisole may be released into the environment through various waste streams by dyes and pharmaceuticals manufacturing facilities. *o*-Nitroanisole has been found in drinking water. Neither volatilization nor biodegradation are expected to be important processes. When released into water, *o*-nitroanisole may adsorb to sediments and suspended solids. Volatilization will be very slow, as the half-life from a model river is approximately 105 days and from a model pond is approximately 772 days. *o*-Nitroanisole will not bioaccumulate in aquatic organisms (HSDB, 1996). *o*-Nitroanisole has moderate mobility when released to soil. *o*-Nitroanisole will remain in vapor phase in the ambient atmosphere. It is degraded in the atmosphere by reactions with photochemically produced hydroxyl radicals, with an estimated half-life of 109 hr.

#### REGULATIONS

Atmospheric emissions are regulated by the U.S. EPA under the Clean Air Act. *o*-Nitroanisole is listed in 40 CFR 63 Subpart F (Organic chemical manufacturing industry) and 40 CFR 60.489(a) (Stationary source standards). Regulations are summarized in Volume II, Table B-90.